GENENT.046DV1 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Ingrid W. Caras	Group Art Unit Unknown
Appl. No.	:	Unknown (Divisional of App. No. 08/635,130, filed April 19, 1996)	I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D C 20231, on
Filed	:	Filed Herewith	December 6, 2001 (Date)
For	:	AL-2 NEUROTROPHIC FACTOR	Ginger R. Dreger, Reg. No. 33,055
Examiner	:	Unknown	

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

The present Preliminary Amendment is filed concurrently with the filing of the above-identified divisional application. Please amend this application in the following aspects:

In the Specification:

Please rewrite the paragraph bridging pages 5 and 6 to read as follows:

--Figure 1A-1B shows the AL-2l-encoding nucleotide sequence (SEQ ID NO: 1), its complementary sequences, and the deduced amino acid sequence of AL-2 of the isolated AL-2l ("AL-2 long") cDNA (SEQ ID NO: 2). The deduced N-terminus of the mature AL-2 protein begins with glycine-27 as numbered from the initiation methionine. The C-terminal hydrophobic transmembrane domain extends from amino acid Leu-220 to Ala-245. The deduced extracellular domain sequence includes aminoacids Gly-27 to Pro-219.--

On page 6, please rewrite the paragraph starting at line 5 to read as follows:

-- Figure 2A-2B shows the AL-2s-encoding nucleotide sequence (SEQ ID NO: 3), its complementary sequence, and the deduced amino acid sequence (SEQ ID NO: 4) of AL-2 of the isolated AL-2s ("AL-2 short") cDNA. The deduced N-terminus of the mature AL-2 protein begins with glycine-27 as numbered from the initiation methionine. The C-terminal hydrophobic transmembrane domain extends from amino acid Leu-220 to Ala-245. The deduced extracellular domain sequence includes amino acids Gly-27 to Pro-219.--

On page 6, please rewrite the sentence starting at line 10 to read as follows:

--Figure 3A-3B depicts an alignment of the AL-2l nucleotide sequence with human EST sequence H10006 (SEQ ID NO: 5).--

On page 6, please rewrite the paragraph starting at line 12 to read as follows:

-- Figure 4 shows a comparison of the AL-2l and AL-2s amino acid sequences with that of Lerk2 (SEQ ID NO: 9) (Beckmann *et al., EMBO J.*, 13:3757-3762 (1994)) and human Htk-L (SEQ ID NO: 10) (Bennett *et al., Proc. Natl. Acad. Sci. USA*, 92:1866-70 (1995); WO 96/02645 published February 1, 1996; both are incorporated by reference herein). Identical amino acids are boxed, and gaps introduced for optimal alignment are indicated by dashes. Conserved cysteine residues can be seen. The deduced C-terminal amino acid for AL-2s is valine.--

On page 6, please rewrite the paragraph starting at line 17 to read as follows:

--Figure 5 shows a comparison of the AL-2l amino acid sequences with that of Lerk2 (SEQ ID NO: 9) and human Htk-L (SEQ ID NO: 10). Identical amino acids are boxed, and gaps introduced for optimal alignment are indicated by dashes. Conserved cysteine residues can be seen.--

On page 27, please rewrite the paragraph starting at line 27 to read as follows:

--In designing the chimeras of the present invention domains that are not required for neurotrophin binding and/or biological activity may be deleted. In such structures, it is important to place the fusion junction at residues that are located between domains, to avoid misfolding. With respect to the parental immunoglobulin, a useful joining point is just upstream of the cysteines of the hinge that form the disulfide bonds between the two heavy chains. In a

frequently used design, the codon for the C-terminal residue of the 'adhesin' part of the molecule is placed directly upstream of the codons for the sequence DKTHTCPPCP (SEQ ID NO: 6).--

Please replace the paragraph bridging pages 63 and 64 with the following rewritten paragraph:

--Two 60-mer oligonucleotide probes were designed based on the sequence of the EST 10006, namely sense-probe-H1006 (5'-GGA CAA AGT CCC GAG GGG CTG TCC CCC GAA AAC CTG TGT CTG AAA TGC CCA TGG AAA-3') (SEQ ID NO: 7) and antisense-probe-H1006 (5'-CAG GTT CTC CTT CCC CAG GCT CCC AGG CTG TGG GCT GCC CCT CCT CGG TCT CTT TCC ATG GGC-3') (SEQ ID NO: 8).--

In the Claims:

Please cancel claims 1-34, and 36-39, without prejudice.

Please amend claim 35 to read as follows:

35. (Amended) A method for accelerating neovascularization of a wound, comprising applying to the wound an angiogenically effective amount of a pharmaceutical composition comprising an isolated polypeptide having an amino acid sequence that is at least 85% homologous to the mature human AL-2 amino acid sequence shown in Figure 1A-1B (SEQ ID NO: 2) or Figure 2A-2B (SEQ ID NO: 4) and a physiologically acceptable carrier.

Please add the following new claims:

--40. (New) The method of claim 35 wherein said wound is due to surgical incision, burn, traumatized tissue, skin graft, or ulcer.

41. (New) The method of claim 35 wherein normal healing of said wound is retarded.

42. (New) The method of claim 41 wherein the retardation is due to advanced age, diabetes, cancer, or treatment with an anti-inflammatory drug or an anticoagulant.

43. (New) The method of claim 35 wherein said composition is a topical composition.

44. (New) The method of claim 43 wherein said topical composition is in the form of an irrigant or salve.

45. (New) The method of claim 35 wherein said composition is contained in a suture, graft, or dressing.

46. (New) The method of claim 35 wherein said composition is a sustained release composition. --

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Please charge any additional fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 6, 2001 By: _____

Ginger R. Dreger
Registration No. 33,055
Attorney of Record
620 Newport Center Drive
Sixteenth Floor
Newport Beach, CA 92660
(415) 954-4114

Version with markings to show changes made

In the Specification:

The paragraph bridging pages 5 and 6 has been amended as follows:

--Figure 1A-1B shows the AL-2l-encoding nucleotide sequence (SEQ ID NO: 1), its complementary sequences, and the deduced amino acid sequence of AL-2 of the isolated AL-2l ("AL-2 long") cDNA (SEQ ID NO: 2). The deduced N-terminus of the mature AL-2 protein begins with glycine-27 as numbered from the initiation methionine. The C-terminal hydrophobic transmembrane domain extends from amino acid Leu-220 to Ala-245. The deduced extracellular domain sequence includes aminoacids Gly-27 to Pro-219.--

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In the Claims:

Claims 1-34, and 36-39 have been canceled, without prejudice.

Claim 35 has been amended as follows:

35. (Amended) A method for accelerating neovascularization of a wound, comprising applying to the wound an angiogenically effective amount of [the] a pharmaceutical composition [of claim 28] comprising an isolated polypeptide having an amino acid sequence that is at least 85% homologous to the mature human AL-2 amino acid sequence shown in Figure 1A-1B (SEQ ID NO: 2) or Figure 2A-2B (SEQ ID NO 4:) and a physiologically acceptable carrier.

The following new claims have been added:

--40. (New) The method of claim 35 wherein said wound is due to surgical incision, burn, traumatized tissue, skin graft, or ulcer.

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45. (New) The method of claim 35 wherein said composition is contained in a suture, graft, or dressing.

46. (New) The method of claim 35 wherein said composition is a sustained release composition. --

Transfer request

PATENT
GENENT.046DV1
Date: December 4, 2001

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Appl. No.	:	Unknown (Continuation of U.S. No. 08/635,130, filed on April 19, 1996)	I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C 20231, on
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For	:	AL-2 NEUROTROPHIC FACTOR	Ginger R. Dreger, Reg. No 33,055
Examiner	:	Unknown	

REQUEST TO TRANSFER COMPUTER READABLE FORM FROM PRIOR APPLICATION PURSUANT TO 37 C.F.R. 1.821(e)

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

The paper copy of the Sequence Listing in this application, is identical to the computer readable copy of the Sequence Listing filed in application Serial No. 08/635,130, filed on April 19, 1996. In accordance with 37 C.F.R. 1.821(e), please use the last-filed (January 5, 1998) computer readable form in that application as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary change in application number and filing date for the instant application. A paper copy of the Sequence Listing is incorporated into the specification.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 6, 2001

By: _____
Ginger R. Dreger
Registration No. 33,055
Attorney of Record

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